Czech Childhood Obesity Population Analysis: Correlation between Anthropometric and Genetic Data.

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INTRODUCTION:

Increasing prevalence of obesity manifested during growth already focused attention on main factors responsible for this serious health problem. The role of genetics has been studied during last decades, especially due to further development of methods which enable to explain main cause of hereditary factors. In the Czech Republic obese children were treated both in pediatric hospitals, endocrinological departments and special ambulances for the obese since the forties - fifties of the last century. Mostly efficient treatment was always found after in-patient treatment in pediatric clinics, and/or in special summer camps. Also treatment in spa centres for childhood obesity treatment has given satisfying results.Obese boys and obese girls were followed before and after reduction treatment (5 weeks) in the spa Podebrady. Anthropometric, body composition, biochemical, hormonal etc. parameters were checked. Selected children were also followed from the point of view of genetic factors in the Department of Anthropology and Human Genetics, Faculty of Science, Charles University in Prague and Institute of Endocrinology. Their characteristics are given in tables. Five genetic polymorphisms and their impact on the status of obese children and the result of their treatment was followed and analyzed :1) PPARgamma2 (peroxisome proliferator- activated receptor gamma 2) was proved as important regulator of adipogenesis.

UCP1 (uncoupling protein 1) uncouples the flow of electrons, which joins the proces of aerobic respiration with translocation of hydrogen ionts into intermembrane space, from oxidative phosphorylation. Therefore, energy of the oxidized substrates is not deposited in the form of ATP, but released as heat. Frequency representation of UCP1 in obese children is presented in Tables 2a, 2b, 2c.Gene B2AR (beta – 2 – adrenoreceptor) plays an important role e.g. in the stimulation of thermogenesis, and activation of lipomobilization in the adipose tissue. B2AR is a dominant lipomobilizaton factor in the adipose tissue. Polymorphism Gln27Glu is associated with obesity, and also with hypertriglyceridemia and diabetes 2 (Tables 3a,3b). Gene FABP2 (fatty acid binding protein 2) includes several types of proteins, and some of them (size 14-15kDa) have a role in cell metabolism and in the transport of long chain fatty acids. Some studies showed the association with the amount of visceral fat, BMI and percentage of body fat). Frequency see in Tables 4a,4b. Gene INS VNTR (insuline, variable number of tandem repeats) (synonyms -insuline minisatellite, insulin - related VNTR, insulin - linked polymorphic region – ILPR). Length variability INS VNTR is connected, inter alia, also with obesity). Frequency representation see in Table 5a,5b.

METHODS:

Following molecular genetic methods were performed: isolation of nucleic acid from peripheral blood leucocytes, polymerase chainreaction with specific oligonucleotide pairs, polyacrylamide DNA fragment separation, restriction fragment length polymorphism techniques with specific restriction endonucleases

A complete **anthropometric examination** was made at the beginning and end of a five-week stay in the spa by the standard anthropometric technique according to Martin and Saller or its modification. The skinfold thickness was assessed by a Best caliper, as the Harpenden caliper has a range of the arms of only 40 mm and therefore its use in the obese population is limited.

Tab.1: PPARgama polymorphism

	Pro/Pro	Pro/Ala	Ala/Ala
Controls (n=114)	88 77%	26 23%	0 0%
Obese subjects (n=299)	225 75%	71 24%	3 1%

PPARgamma2 (peroxisome proliferator-activated receptor gamma 2) was proved as the main regulator of adipogenesis ; its polymorphisms Pro2Ala and Pro115Glu were followed, due to their association with obesity which contributes to the variability of the amount of adipose tissue and the ability to react to insulin. However, conclusions of further studies are not synonymous.Frequency representation of PPARgamm2 in groups of obese as compared to control children did not differ. (Tab. 1)

PATIENTS:

In the period 2001 – 2009 the authors analyzed czech obese youth population in selected genetic polymorphisms and they evaluated correlation between elementary anthropometric parameters and tested genetic polymorphisms.

RESULTS:

Frequency of UCP1 gene in groups of control and obese subjects

UCP1 genotyp	A/A	A/G	G/G
controls n	59	45	10
%	52	39	9
obese n	153	126	23
%	51	42	8

χ^2 = 0.26 df = 2 p = 0.88

Gene UCP1, polymorphism A-3826G, in boys lower weight reduction and smaller increase of the percentage of muscles were observed in boys - carriers of rare genotype GG, as compared with more common genotype AA . Rare genotype GG was associated with quantitatively smaller success of reduction treatment in obese boys in a quantitative sense, as well as in the changes of body composition.

Tab.2a: Increase in muscle mass (%) after reduction treatment in carriers of gene UCP1, polymorphism A-3826 (obese boys)

UCP1 genotype	x	SD	p
AA	3.83	2.73	
AG	2.30	2.59	
GG	1.18	3.36	0.020*

Tab.2b: Weight reduction (%) after treatment in carriers (obese boys) of gene UCP1, polymorphism A-3825

Weight reduction %

UCP1 genotype	x	SD	p
AA	10.52	2.56	
AG	10.72	2.62	
GG	9.25	3.25	0.040*

Tab.3a: Weight reduction (%) after treatment in carriers of gene Beta 2AR (obese girls)

Beta 2AR genotype	x	SD	p
Gln/Gln	9.28	3.12	
Gln/Glu	9.83	2.86	0.004*
Glu/Glu	8.06	3.12	0.024*

In both genders, smaller change in after reduction treatment was found when **allele Glu – gene Beta 2AR** was present.

In boys, homozygotes Glu/Glu had significantly smaller percentual reduction of abdomen circumference as compared to homozygotes Gln/Gln. In girls, significantly smaller percentual weight reduction inhomozygotes Glu/Glu as compared to heterpzygotes, but also between heterozygotes Gln/Gln was revealed. Allele Glu in genotype was associated with smaller results of reduction treatment both in girls and boys.

Tab.3b: Frequency of BETA2AR gene in groups of control and obese subjects

BETA2AR genotype		Gln/Gln	Gln/Glu	Glu/Glu
Controls	n	33	61	20
	%	29	54	18
Obese	n	127	137	47
	%	41	44	15

χ^2 = 5.05 df = 2 p = 0.08

Tab.4a: Weight reduction (%) in carriers of gene FA BP2, polymorphism Ala 54 Thr (obese girls)

FA BP2 genotype	x	SD	p
Ala/Ala	9.70	2.89	
Ala/Thr	9.37	3.00	
Thr/Thr	7.65	3.77	0.049*

With regard to the role of **gene FABP2, polymorphism Ala54Thr**, in the group of obese girls – homozygotes Thr/Thr a smaller weight reduction was observed as compared to homozygotes Ala/Ala. Genotype Thr/Thr can reduce the effect of reduction treatment in girls, but not in boys.

As apparent, in obese children no differences in the distribution of polymorphisms of mentioned genes were found as compared to controls. In any case, there was also no association of these genes with anthropometric and biochemical parameters in our growing obese subjects.

Tab.4b: Frequency of gene FABP2 in groups of control and obese subjects

FABP2 genotype		Ala/Ala	Ala/Thr	Thr/Thr
Controls	n	56	52	6
	%	49	46	5
Obese	n	159	133	29
	%	50	41	9

χ^2 = 1.84 df = 2 p = 0.40

Tab.5a: Fat reduction (%) in carriers of gene INS VNTR lenght polymorphism (obese girls)

INS VNTR genotype	x	SD	p
1/1	4.94	3.24	
1/3	6.19	3.23	0.049*
3/3	6.48	3.85	

In girl carriers **of gene INS VNTR, length polymorphism,** greater percentual fat reduction after treatment was found in heterozygotes 1/3, as compared to homozygotes 1/1. (Tab. 5a, 5b). These result indicate that the presence of long alleles in genotype might influence positively the results of reduction treatment in obese girls; in boys, no difference was revealed.

Tab.5b: Frequency of IVS VNTR gene in groups of control and obese subjects

INS VNTR genotype		1/1	1/3	3/3
Controls	n	59	52	8
	%	50	44	7
Obese	n	216	153	30
	%	54	38	8

χ^2 = 1.23 df = 2 p = 0.54

Selected anthropometric parameters at the beginning and end of reduction treatment (5 weeks) in a spa Poděbrady (boys, n=180, girls, n=345)

Anthropometric parameters	Initial values			Final values		
	x	SD	z-score	x	SD	Z - score
Age (years)	12,61	2,31		12,71	2,26	
Weight (kg)	77,6	19,71	3,99	69,5	19,84	2,87
Height (cm)	160,3	13,86	0,72	160,4	13,78	0,65
BMI (m/kg^2)	29,59	4,46	4,10	26,42	4,01	2,92
WHR	96,7	5,29		95,0	5,33	
Fat (%) (Matiegka)	37,27	5,76,3	3,47	31,09	5,96	2,37
Reduction of weight (%)	3,58	5,25		4,14	5,20	
Sum of 10 skinfolds (mm)	214,7	41,93		168,2	38,84	
Fat (%) (Pařízková)	22,8	2,90	1,81	20,2	2,38	1,35
Abdominal circumference (cm)	98,3	12,43	4,65	91,9	12,12	3,62
Gluteal " "	101,7	12,12	3,60	96,7	11,35	2,72
Arm relax. " "	30,0	4,08	3,05	28,0	3,77	2,18
Thigh " "	56,9	7,24	3,29	53,8	6,69	2,49

Selected anthropometric parameters – Control groups of men (n=45) and women (n=74)

Anthropometric parameters /men/	mean	SD
age	29,21	7,57
Body weight (kg)	76,83	11,44
Body height (cm)	182,11	5,84
BMI (m/kg^2)	23,05	2,99
Rohrer's index	1,27	0,14
WHR index	82,0	5,0
Fat (kg) Matiegka	12,34	2,30
Fat (%) Matiegka	15,81	6,56
Muscles (kg) Matiegka	35,72	4,22
Muscles (%) Matiegka	46,49	4,03
Weist circum. (cm)	80,97	8,26
Abdominal circum. (cm)	84,68	8,26
Glutelal circum. (cm)	98,34	60,3

Anthropometric parameter	Initial values			Final values		
	x	SD	z-score	x	SD	Z - score
Age (years)	13,24	2,61		13,34	2,62	
Weight (kg)	74,0	16,28	3,86	67,3	14,67	2,87
Height (cm)	159,1	11,35	0,59	159,2	11,34	0,56
BMI (m/kg^2)	28,96	4,39	4,10	26,2	3,95	3,94
WHR	89,5	7,0		87,6	6,31	
Fat (%) (Matiegka)	36,01	6,25	3,93	30,04	5,82	2,54
Weight reduction x	1,06 %	6,59		0,65 %	6,29	
Sum of 10 skinfolds	201,6	42,23		160,4	35,00	
Fat (%) (Pařízková)	29,2	3,68	2,85	25,5	3,94	2,02
Abdominal circumference (cm)	92,8	11,11	3,46	86,5	10,20	2,54
Gluteal " "	103,9	11,21	3,37	98,9	10,52	2,53
Arm relax. " "	29,1	3,12	2,78	27,2	2,84	1,93
Thigh " "	21,9	2,60		21,3	1,80	

Anthropometric parameters /women/	mean	SD
Age (years)	33,46	11,92
Body weight (kg)	63,31	90,4
Body height (cm)	167,37	6,13
BMI (m/kg^2)	22,62	3,13
Rohrer's index	1,35	0,13
WHR index	74,0	6,0
Fat (kg) Matiegka	15,10	5,45
Fat (%) Matiegka	23,85	7,36
Muscles (kg) Matiegka	25,36	4,10
Muscles (%) Matiegka	40,66	3,97
Weist circum. (cm)	72,08	8,12
Abdominal circum. (cm)	78,62	8,27
Gluteal circum. (cm)	97,92	5,84

CONCLUSION:

However, **selected polymorphisms**, e.g. rare genotype GG - gene UCP1 in boys, or presence of allele Glu in gene Beta2AR in both genders, or genotype Thr/Thr - FABP2 in girls were **associated in our groups of obese children with smaller success of the same reduction treatment.** On the contrary, e.g. the presence of long alleles in genotype INS VNTR showed **positive influence** the results of reduction treatment. We observed following genetic and anthropmetric correlations:

- **lower occurrence of genotype 1/3 in VNTR region of INS gene – Czech childhood obese population**
- **lower occurrence of Gln homozygotes and higher occurrence of Gln/Glu heterozygotes in Czech childhood obese population (correlation wtih Czech control group)**
- **no evidence of differencies of allele or genotype frequencies in FABP2 and UCP1 gene**
- **lower body weight in Czech childhood obese population with FABP2 and beta 2 adrenergic receptor genes**

As apparent, the reactivity of the organism to the same treatment can vary significantly with regard to genetic endowment. But with proper knowledge about the effect of genetic predispositions the treatment could achieve better and especially lasting effects, which would be desirable from the point of view of health prognosis for later life, and also prevention of the essential predisposing factor - obesity starting since childhood.

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